REMARKS

Status of the Claims

Claims 21-23 and 32-34 are pending in the present application.

Claims 21-23 and 32-34 were rejected and claim 21 was objected to.

Claim 21 has been amended.

Upon entry of this response claims 21-23 and 32-34 will be pending.

Summary of the Amendment

Claim 21 has been amended to define the invention more clearly and place the claims in better condition for allowance. Support for the amendment appears throughout the specification and the claims as originally filed.

No new matter has been added.

Claim Objections

Claim 21 is objected to for failure of the claim to recite the full name of HIV Vpr protein. The claim has been amended to spell out the full name of the protein prior to use of the acronym "Vpr." The claim as amended recites the invention more precisely. Applicants respectfully request that the objection of the claim be withdrawn.

Claim Rejections under U.S.C. § 112, first paragraph

Claims 21 – 23 and 32 – 34 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing the enablement requirement. The Office asserts that claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

In support of the Office assertion, the Office states:

> the disclosure is silent pertaining to specific method steps of inhibition and prevention of lymphocyte activation. The disclosure fails to provide any guidance pertaining to the structural

> characteristics or mechanisms of interaction between Vpr and lymphocytes

(Office Action, page 5-6). Applicants respectfully disagree and traverse.

Applicants note that it is well established that the Office has the initial burden of establishing that a claimed invention does not meet the enablement requirement. The description of the invention is presumed to be enabled and, in order to sustain an enablement rejection under the first paragraph of 35 U.S.C. § 112, the Examiner must establish doubt in the objective truth of Applicant's assertion that the claimed invention is enabled using reasoning and evidence of those skilled in the art. See, e.g. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). See also M.P.E.P. § 2163.

The Office has failed to set forth any reasoning or evidence to support the rejection. The Office has not established that the claimed invention does not meet the enablement requirement. Failing to do so, the burden is not properly shifted to Applicants. Applicants respectfully urge that the evidence and reasoning in the specification supports the conclusion that one skilled in the art would accept Applicant's assertion that the claims are enabled by the specification. In the absence of any evidence and reasoning in support of the rejection, Applicants are not required to put forth any evidence.

Applicants respectfully request that any rejection based upon the Office statement above be withdrawn as the statements are not an accurate representation of the content of the specification. The Office has failed to provide any objective evidence or reasoning to question the validity of the contents of the specification. The Office has failed to present a single cited reference that demonstrates the claimed invention would not work. The Office has, instead, chosen to assert conclusory remarks about what one of ordinary skill in the art would not know based upon a negative inference drawn from references that do not discuss Vpr activity. The Office reasoning is therefore flawed and the evidence provided by the Office is not relevant.

In further support of the Office assertion, the Office states that:

> The prior art is unpredictable and fails to provide sufficient illumination pertaining to the mechanisms underlying inhibition and prevention of lymphocyte action by the Vpr protein

(Office Action, page 6). Applicants note that the correct standard for whether claims are enabled is whether the specification discloses one method to practice the claimed invention that bears a reasonable correlation to the entire scope of the claims. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ18, 24 (CCPA, 1970). Applicants urge that the specification bears a reasonable correlation to the scope of he claims.

Applicants respectfully urge that one of ordinary skill in the art could practice the claimed invention by reading the specification. Claims 21-23 refer to methods of preventing lymphocyte activation. The steps set forth in claim 21 include "obtaining isolated Vpr protein" and

> contacting lymphocyte cells with an amount of said Vpr protein effective to prevent activation

Claims 32-34 refer to methods of inhibiting lymphocyte activation. Claims 32-34 include the step of "obtaining isolated Vpr protein" and the step of:

> contacting lymphocyte cells with an amount of said Vpr protein effective to inhibit activation; wherein cytokine production and secretion by immunoglobulin activation of lymphocyte cells is inhibited

In describing the methods, the specification clearly discloses that Vpr prevents lymphocyte activation as well as cell proliferation. For example, on page 9 lines 11-14 of the specification states:

> It has been discovered that HIV protein vpr inhibits cell proliferation, induces undifferentiated cells to differentiate, that vpr effects modifies the state of macrophage cells, and prevents activation of lymphocytes.

Page 10, lines 14-20, of the specification clearly describes what happens when activation is inhibited or prevented, stating

> It has been discovered that activation of lymphocytes such as T cells, B cells and monocytes can be inhibited by Vpr. Vpr prevents activation of these cells by immunoglobulin molecules. Activation of these cells by immunoglobulin molecules results in cytokine

> production/secretion. Accordingly, Vpr inhibits cytokine production/secretion by these cells due to immunoglobulin activation.

The specification specifically discloses that Rip-1 is found in lymphocytes. (Specification, page 46, lines 25-37). The specification specifically discloses that steroids interact with Rip-1. (Specification, page 48, lines 10-37). The specification specifically discloses that Vpr interacts with Rip-1. (Specification, page 49, lines 1-21). It is was commonly known at the time of filing the application that hydrocortisone and dexamethasone inhibit activation of lymphocytes. The specification demonstrates that administration of hydrocortisone, dexmethasone, or Vpr result in Rip-1 translocation to the nucleus. (Specification, pages 50-52). The glucocorticoid steroid receptor antagonist on the other hand, RU486, has been demonstrated to inhibit activation of lymphocytes by specifically preventing dexamethasone, hydrocortisone and Vpr from inducing translocation of Rip-1 to the nucleus. (Specification, pages 50-53). The specification specifically demonstrates that GC receptor antagonists inhibit the effects of Vpr-induced interactions with Rip-1. (Specification, pages 50-53). Therefore, one skilled in the art would only have to read the specification in order to practice to claimed invention. The specification fully supports the claims.

The claims are enabled. Applicants respectfully request that the rejection of claims 21-23 and 32-34 based upon 35 U.S.C. §112, first paragraph, be withdrawn.

Conclusion

Claims 21-23 and 32-34 are in condition for allowance. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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